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Research Article

Evaluation of prescription pattern and compliance in Kashmiri women with Polycystic Ovarian Syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrine system disorder affecting women of reproductive age. As there are a few studies with inconsistent data available in the literature regarding the prescription pattern and compliance of drugs in patients with PCOS, both within and outside India, the present study was undertaken to generate some valid and useful data regarding these parameters.

Objective: Evaluation of drug utilization and assessment of prescribing patterns and patient compliance among Kashmiri women with polycystic ovary syndrome.

Materials and Methods: This study was a prospective, observational and cross-sectional study, which was carried out on Kashmiri females diagnosed with PCOS as per Rotterdam criteria of 2003. Patients attending Srinagar based hospitals and clinics over a period of nine months were enrolled in the study. Information was collected through personal interviews using a pre-validated, self-administered data collection tool. The prescribing patterns of drugs were evaluated by comparison with Endocrine Society Clinical Practice Guidelines. Patient compliance with prescribed medicines was assessed using modified Morisky 8-Item Medication Adherence Questionnaire.

Results: Drugs prescribed to the study patients included oral contraceptive pills (OCPs) 57(46.34%), insulin sensitizers 75 (60.97%), anti-androgen 37 (30.08%), anti-estrogens 1 (0.81%), progestins 10 (8.13%), dopaminergic agonists 7 (5.69%), steroids 2 (1.62%) and statins 1(0.81%). 50 (40.65%) patients were highly adherent to their prescribed medications. **Conclusion:** The study revealed that nature of drugs prescribed to the study population was in consonance with the established standard guidelines. Most of the women were highly adherent to their prescribed medications.

Keywords: PCOS, prescription, drug adherence.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrinological disorder, affecting 5–10% of women of reproductive age¹. It is marked by chronic anovulation, hyperandrogenism and/or polycystic ovarian morphology². There is a spectacular increase in the prevalence of PCOS all over the world especially in Asia. Prevalence of PCOS differs depending upon the criteria used. Prevalence of PCOS in Indian adolescents and young girls in 2014 was about 22.5% by Rotterdam and 10.7% by Androgen Excess Society criteria³.

Drug prescribing is frequently the finished end result of most medical consultations^{4,5}. Since great quality prescriptions are essential for the accurate dispensing of medicines and contribute to minimizing medication errors,

doctors ought to adhere to the guidelines of prescription writing for the advantage of the patient. Prescription pattern in PCOS patients has not been studied widely and it needs to be evaluated. Since PCOS is the heterogeneous condition of varied etiology, the therapeutic options may also differ widely, and therefore need to be individualized to address the predominant manifestations and defined therapeutic objectives. There is paucity in published literature with regard to the prescription pattern of PCOS all over the world including India. A few studies have been conducted on the incidence, prevalence, etiology, epidemiology and biochemical profile of PCOS among Kashmiri population, but no study has been published regarding evaluation of drug utilization among these patients.

MATERIALS AND METHODS

This prospective, observational and cross-sectional study was carried over a period of nine months from Srinagar based hospitals and clinics from September, 2014 to May, 2015.

Patients diagnosed with PCOS as per Rotterdam criteria 2003 were enrolled in the study. 123 patients of all age groups were included and all patients who did not receive any drugs were excluded from the study. Patients with PCOS as per Rotterdam criteria 2003 attending departments of endocrinology/gynaecology/dermatology of Srinagar based hospitals and private clinics and those attending health camps organized at the University of Kashmir were recruited in the study.

Data collection

Informed consent was obtained from all the study subjects. All the patients included in the study had PCOS as per Rotterdam criteria 2003⁶ (Rotterdam, 2003). Study and patient specific data was collected from medication charts and prescriptions. Consonance of clinical practice, vis-à-vis pharmaco-therapeutic management of PCOS, with established guidelines among the study patients using prefixed criteria in accordance with published literature was evaluated. Data was collected, analyzed and evaluated for evolving an overall picture about the drug utilization practices among the study subjects. Prescription patterns in the study patients were evaluated by collecting details of the drug therapies prescribed i.e., the therapeutic class of drugs used, dose, route, frequency and duration of therapy. Information was collected through personal interviews using a pre-validated, structured data collection form. Pre-validation of the data collection form was done on a group of doctors dealing with PCOS patients, incorporating their suggestions for improving the clarity, comprehensibility, unambiguity and relevance of the questions asked in the data collection form. Patient compliance with prescribed medicines was assessed using modified Morisky 8-Item Medication Adherence Questionnaire⁷. The questionnaire consists of a set of eight questions having a 'Yes or No answer'. Each question answered in affirmative was given a score of 1 and the question answered in negative was given a score of 0 and the overall score was calculated. The overall score of '0' indicated high adherence, '1 or 2' indicated medium adherence and a score '>2' indicated low adherence. Reasons for non-adherence to prescribed medications was identified from the patient interviews upon counseling and accordingly documented. The drug related problems, patients response to the treatment and therapeutic outcome of the study patients were evaluated through their personal interviews using structured data collection form.

Feedback was obtained from the practising physicians regarding their prescribing preferences for PCOS patients using a structured and pre-validated questionnaire. This helped in the assessment of their knowledge, attitude and practices in care of PCOS. Further the prescribing practices of the practising physicians and their adherence to the prescribed guidelines were evaluated by comparing with Endocrine Society Clinical Practice Guidelines 2013⁸ and it was ascertained whether prescribing in PCOS patients was as per the established guidelines or not.

Statistical Analysis

Statistical Analysis of the data was carried out using GRAPHPAD INSTAT (version 3.1) and SPSS (version 16) software. The results were depicted in the form of percentages. Significance of the differences observed among

various variables and outcome measures was ascertained by calculating p-values using chi-square test. P values < 0.001 were deemed to be highly significant.

RESULTS

Out of 123 in the study, 31 (25%) patients were married and 92 (74.97%) patients were unmarried. The mean age of the study patients was 23.70 ± 0.41 years and the mean age at menarche was 13.06 ± 0.15 years. Prescription pattern of study patients revealed that 57(46.34%) had OCPs prescribed, 75(60.97%) insulin sensitizers, 37(30.08%) anti-androgen, 1(0.81%) anti-estrogen, 10(8.13%) progestins, 7(5.69%) dopamine agonist, 2(1.62%) steroids, 2 (1.62%) steroids and 1(0.81%) had statins prescribed as shown in Fig 1. Among OCPs prescribed in married population 6(10%) were prescribed with E.E +Drospirenone, 2(3.5%) E.E+Cyproterone acetate, 2(3.5%) E.E+Norgestral and 0(0%) with E.E+Desogestral and in unmarried population 23(40.3%) were prescribed E.E+Drospirenone, 09(15.7%) E.E+Cyproterone acetate, 12(21%) E.E+Norgestral and 03(5.2%) E.E+Desogestral with P value of >0.001 as shown in Fig 2.

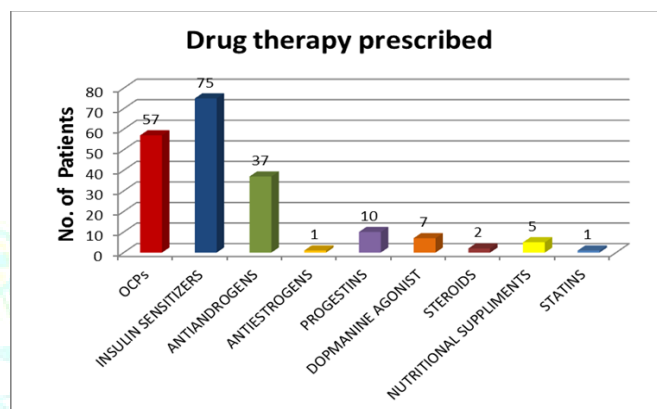


Fig 1: Drug therapy prescribed to the Study patients:

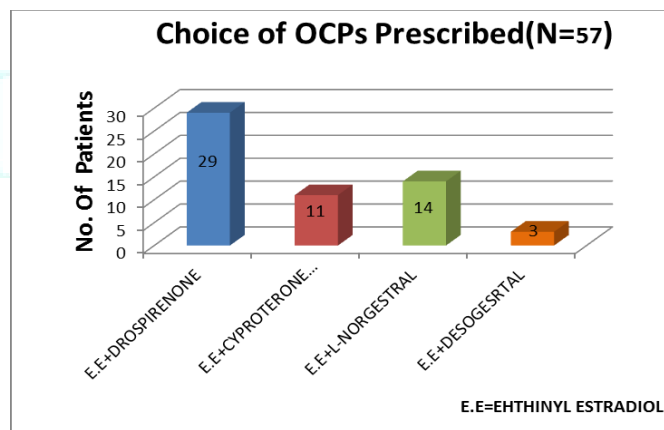


Fig 2: Choice of oral contraceptives prescribed to the study patients

Among insulin sensitizers, 16(21.3%) were prescribed metformin, 3(4%) pioglitazone, 5(6.6%) myo-inositol and 1(1.3%) metformin+myo-inositol in married population. Among unmarried population, 40(53.3%) were prescribed metformin, 4(5.3%) pioglitazone, 3(4%) myo-inositol, 2(2.6%) metformin+myo-inositol and 1(1.3%) metformin+sitagliptin with the P value of >0.001 as shown in Fig 3.

Adherence of the patients towards their medication was calculated using Morisky score. It was found out that 50 (40.65%) of the patients were highly adherent to their medication, 41(33.33%) patients had medium adherence

and 32 (26.01%) patients were poorly adherent to their medication as shown in Table-1. Reasons given by patients upon counseling for non-adherence to prescribed medication revealed that 65.5% patients' had drug intolerance, (18.75%) had lack of information and awareness, and 15.62% patients gave non-affordability as the reason.

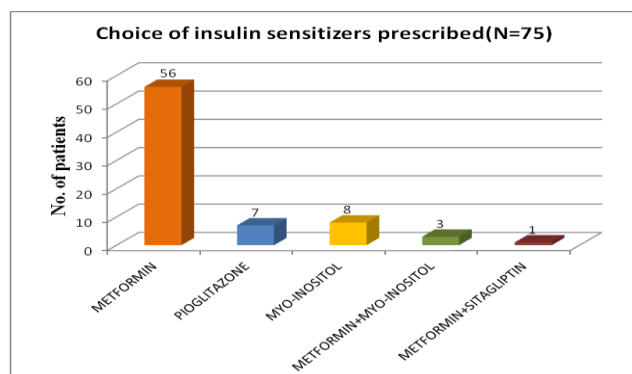


Figure- 3: Choice of insulin sensitizers prescribed to the study patients

In the present study drug related problems were mostly seen with metformin 67%, followed by spironolactone 8.9% and others. Out of 123 patients with PCOS, 100 (81.3%) patients were satisfied with the prescribed drug therapy,

whereas 23 (18.69%) patients were not satisfied with the prescribed drug therapy. Further Therapeutic outcome of the patients revealed that 91(73.98%) patients had regular menstrual cycles after drug treatment, 49 (39.83%) patients showed decrease in hirsutism, 11 (8.9%) showed decrease in Alopecia, 38 (30.89%) showed decrease in weight, 20(16.26%) showed decrease in Acne, were as 15 (12.19%) had irregular cycles even after drug treatment, followed by 6 (4.8%) patients which had no change in hirsutism, 1(0.8%) had no change in alopecia, 2 (1.62%) had no change in weight and 1(0.8%) had no change in acne after drug treatment.

The Comparison of actual prescribing practices and feedback obtained from physicians with Endocrine Society Clinical Practice (EDCPG) Guidelines of 2013 was done and is shown in Table 2.

Table- 1: Patient compliance to prescribed medications:

MORRISKY SCORE	NO. OF PATIENTS
0	50(40.65%)
1	16(13%)
2	25(20.32%)
>2	32(26.01%)
TOTAL(N)	123

Scores: >2 = low adherence, 1 or 2 = medium adherence, 0 = high adherence

Table-2: Comparison of actual prescribing practices and feedback obtained from physicians with Endocrine Society Clinical Practice (EDCPG) Guidelines of 2013.

Recommendations of Endocrine Society Clinical Practice Guideline (ESCPG) 2015	No. of patients in whom prescribing was found in accordance with given recommendations	No. of physicians whose feedback was in consonance with ESCPG guidelines
Hormonal Contraceptives (i.e., oral contraceptives, patches or vaginal rings) as first-line management for the menstrual abnormalities and hirsutism/acne of PCOS.	Prescribed as first line treatment in 55(44.7%) patients and as second line treatment in 5(4%) patients	20 (80%)
Use of exercise therapy in the management of overweight and obesity in PCOS. Weight loss strategies should begin with calorie-restricted diets (with no evidence that any one type of diet is superior) for adolescents and women with PCOS who are overweight or obese.	120(97%) patients were advised exercise therapy	10 (40%)
Recommendation against the use of Metformin as a first line treatment for cutaneous manifestations, for prevention of pregnancy complications, or for the treatment of obesity.	22(18%) patients were prescribed Metformin as the first line treatment.	7 (28%)
Recommend Metformin in women with PCOS who have T2DM or IGT who fail upon lifestyle modifications. For women with PCOS with menstrual irregularity who cannot take or do not tolerate HCs, suggest Metformin as second-line therapy.	14(11%) patients were prescribed Metformin as the 2 nd line treatment	23(92%)
Recommend Clomiphene citrate (or comparable estrogen modulators such as Letrozole) as the first-line treatment of anovulatory infertility in women with PCOS.	1(20%) patient was prescribed CC as a 1 st line treatment in Anovulatory infertility	3(12%)
Suggest the use of Metformin as an adjuvant therapy for infertility to prevent ovarian hyperstimulation syndrome (OHSS) in women with PCOS undergoing in-vitro fertilization (IVF).	No patient in whom Metformin was used as an adjuvant therapy for infertility to prevent OHSS was detected.	15(60%)
Recommend against the use of insulin sensitizers, such as inositols (due to lack of benefit) or thiazolidinediones (due to safety concerns), for the treatment of PCOS.	Myo-inositol was prescribed in 8(6.5%) patients and thiazolidinediones (Pioglitazone) in 7(5.6%) patients, in contrast to the guidelines.	-
Suggest against the use of statins for treatment of hyperandrogenism and anovulation in PCOS until additional studies demonstrate a favorable risk-benefit ratio.	1(0.81%) such patient was prescribed with statins.	-

DISCUSSION

Present study showed that 43.90% patients with PCOS were in the age-group of 19-24 years and 39.83% patients in the age group of 25-30 years, indicating that PCOS is more common among the women between age groups of 19-30 years. The mean age of study patients was 23.707 ± 0.41 years and mean age at menarche was 13.065 ± 0.1495 years. Most of the previous studies focused upon the similar age groups. Nasr et al in 2004 conducted a study on oligomenorrheic infertile women, & included patients between age group of 21-35 years⁹.

The Endocrine Society Clinical Practice Guidelines for PCOS recommend Hormonal contraceptives (i.e, oral contraceptives, patches, or vaginal rings) as first-line management for the menstrual abnormalities and hirsutism/acne of PCOS. In the present study oral contraceptives, were prescribed as the 1st line treatment in 55 (44.7%) patients and in 5(4%) patients as 2nd line treatment. Further in the study out of 123 patients only 57(46.34%) patients had OCPs prescribed for PCOS indicating that OCPs were not always first line treatment for most of the patients. Badawy and Elnashar in 2011, also reported oral contraceptive pills (OCPs) as first-line treatment for pharmacologic management of hirsutism in premenopausal women¹⁰. Further 20 (80%) practitioners were of the opinion that they prescribe OCPs, as the first line treatment for menstrual disturbance and hirsutism which is in accordance with the guidelines.

In the present study 22(18%) patients were prescribed Metformin as the first line treatment and 14(11%) patients as the second line treatment but Endocrine Society Clinical Practice Guideline for PCOS make recommendation against the use of Metformin as first line treatment for cutaneous manifestations, for prevention of pregnancy complications, or for the treatment of obesity. Guidelines recommend use of Metformin in women with PCOS who have T2DM or IGT and who fail upon lifestyle modifications. Guidelines further recommend Metformin as second-line therapy for women with PCOS along with menstrual irregularity who cannot take or do not tolerate hormonal contraceptives. However in the present study oral contraceptives were well tolerated as compared to Metformin which was not tolerated well in 62.5 % patients. Further, only 7(28%) practitioners were of the opinion that they prescribe Metformin as the first line treatment, whereas 23 (92%) practitioners preferred it as 2nd line treatment for PCOS. Thus most of the practitioners prescribed Metformin in accordance with these guidelines.

Study showed that, 9.33% patients were prescribed Pioglitazone and 10.66% were prescribed Myo-inositol which is in contrast to the guidelines that recommend against the use of insulin sensitizers, such as inositols (due to lack of benefit) or thiazolidinediones (due to safety concerns), for the treatment of PCOS. In the present study only 0.81% patients had been prescribed statins which is in accordance with the guidelines that suggest against the use of statins for treatment of hyperandrogenism and anovulation in PCOS unless additional studies demonstrate a favorable risk-benefit ratio. However guidelines suggest statins in women with PCOS who meet current indications for statin therapy. In the present study out of 123 patients 1(0.81%) patient had anti-estrogen Clomiphene citrate prescribed for PCOS which is in accordance with the existing guidelines that recommend Clomiphene citrate (or comparable estrogen modulators such as Letrozole) as the first-line treatment for anovulatory infertility in women with PCOS. In the present study 30.08% had been prescribed anti-androgen Spironolactone as 91.86% patients had mild

hirsutism and 2.43% had moderate to severe hirsutism. In this study OCPs were prescribed among 46.34% patients. The choice of OCPs prescribed to study patients showed that only 11(19.29%) patients were prescribed E.E+Cyproterone acetate which is in contrast to the study conducted by Falsetti et al., in 2001 in which 140 patients were prescribed E.E+cyproterone combination¹¹. Similarly studies by Mastorakos et al., in 2002 showed that 14 patients were given E.E+cyproterone combination¹². Thus present study shows that Ethinylestradiol and cyproterone acetate combination has not been widely used in PCOS patients. In this study 29(50.87%) patients were prescribed ethinylestradiol (E.E)+Drospirenone whereas the study by Guido et al 2004 reported that E.E+ Drospirenone was prescribed to 15 patients. Thus, present study revealed that E.E+Drospirenone combination has been prescribed frequently in PCOS patients, whereas among other OCPs, 24.56% patients were prescribed E.E+Norgestrel combination followed by E.E+Desogestrel in 5.26% patients. In the present study ethinylestradiol and anti-androgen progestins have been prescribed more. A recent uncontrolled pilot study on 15 PCOS patients reported that treatment with ethinylestradiol (30µg) and Drospirenone (3mg) combination resulted in decrease in androgen levels after 3 months and improvement in hirsutism after 6 months¹³.

Patient compliance to the medications is one of the most important factors which affect the course and prognosis of the disease. High adherence 50(40.65%) in the present study may be mainly due to the fact that most PCOS women feel distressed about the symptoms like hirsutism and acne. Medium 41(33.33%) and poor adherence 32(26.01%) to their medications, which upon counselling was observed that most common reason for the patients' non-adherence to prescribed medications was drug intolerance (65.5%) to the medications and was mainly observed in patients taking Metformin. Similarly Ali and Fonseca in 2012 reported poor compliance to Metformin due to multiple daily dosing and frequent gastro-intestinal side effects¹⁴. Anti-androgen Spironolactone is considered safe at lower doses however at higher doses when used alone it causes irregular menstrual cycles. In the present study 18.9% patients had irregular cycles with Spironolactone. Similar reports by Hagag et al., in 2014 showed that Spironolactone when used alone causes irregular periods in up to 80% of women¹⁵.

CONCLUSION

This study revealed that the nature of drugs prescribed to the study population was in consonance with the established standard guidelines. In most of the cases OCPs were used as a first line treatment and Metformin as the second line treatment for PCOS. Most of the women were highly adherent to their prescribed medications, which was mainly due to the fact that most PCOS women had image issues due to hirsutism and others had menstrual disturbance which may lead to infertility in later life.

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CONFLICTS OF INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article

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